

cal replacement of a long bone where X-ray shows deviations of a small fraction of an inch, but in the tarsal bones, with their confused outlines of cleavage and fracture, and where normally there is overlapping and complex relations of various bones, he is too apt to put on a cast or adhesive strapping, and trust to luck, so long as the external appearance is normal, which it usually is.

On the contrary, repeated efforts should be made to secure an anatomic reposition, always bearing in mind the importance of the sub-astragaloid joint. Each effort should be checked up by the X-ray, using the sound foot for comparison. We can compress or manipulate the fragments, use small nails to hold fragments in place, cut the tendo-Achilles, and do everything possible to get anatomic restoration of the fractured surface, as shown by the X-ray. We know that fractures extending into a joint require the greatest skill and nicety of reposition to get good results. Nine out of ten fractures of the astragalus and os calcis extend into this joint that, although not permitting much motion, yet bears more weight than any other joint of the body. Consequently, if we are just as particular here as anywhere else, then and then only can we hope for a minimum of restriction and muscle-spasm around the sub-astragaloid joint, and consequent pain and disability.

In a recent article by Cotton upon "Results of Fracture of the Os Calcis," after examining twenty-eight cases of compression fracture, due to falls, his conclusions are as follows: "Os calcis fracture is of as serious prognosis (not as to life, but as to use), as fracture of the femur at the hip. Ordinarily speaking, the man who breaks his heel-bone is 'done' so far as his industrial future is concerned."

"Late operations for correction are useful, but far from ideal in results; palliatives (plates, pads, braces and shoe modifications) are usually useless."

"Early conservative treatment gives incredibly poor results."

I saw two cases of direct violence to the foot—one causing an anterior dislocation of the astragalus and foot with it upon the tibia, and the other a bad crush by a heavy pipe. The former had been competently cared for and the dislocation almost completely reduced, but the tenderness at the sub-astragaloid joint will probably require an arthrodesis to cure. Sub-astragaloid arthrodesis for paralytic feet in children has given good results, and I see no reason why it should not give a painless weight-bearing mechanism here. The other case had already gone on to arthrodesis of the ankle-joint, but this has to be done over again, as the foot was supinated too much for weight-bearing, and placed too far forward upon the tibia. The important point to remember in an ankle-joint arthrodesis is to put the foot as far back as possible upon the leg, and in a position midway between pronation and supination, in order that when standing, the foot may come squarely upon the ground.

The accompanying fractures of the scaphoid, cuneiform and fifth metatarsal bones, seen in this series, presented no especial features of interest to the patients, and hence would not to you.

## THE THERAPEUTIC APPLICATION OF HYPERTONIC SALT-SOLUTION IN CONJUNCTION WITH LEUCOCYTIC EXTRACT.

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The question of the relative therapeutic values of leucocytic extract (Archibald) introduced subcutaneously and that introduced intravenously, alone or in conjunction with various hypertonic salt solutions with special reference to its application in the treatment of cases of infections of the blood stream was first called to our attention, by a case of streptococcemia in which a two per cent. magnesium sulphate solution was administered according to the technic of Harrer, together with leucocytic extract which was given as usual subcutaneously. The beneficial effects of this combination were quite marked.

In this case, a post operative septicemia, 400 c.c. of a two per cent. solution of magnesium sulphate given intravenously was used, as soon as a blood culture revealed the presence of the streptococcus, with no benefit. White blood counts before and after the magnesium sulphate solution injections were uniformly low, a fact indicative of a particularly grave prognosis. In order to stimulate an increase in the activity of the leucocytes, leucocytic extract was given in doses of two cubic centimeters daily for a number of days. Following the use of the extract alone there was an increase in the white count of from six to seven thousand to twelve or thirteen thousand, but no marked leucocytosis was obtained. At this time the administration of magnesium sulphate was resumed in conjunction with the Leucocytic Extract with an immediate and decided increase in the leucocyte count and marked improvements in the physical condition of the patient, who continued to improve and went on to complete recovery.

In this case there was no question but that the combination of these two agents was responsible for the improvement and that neither one alone was able to benefit the condition.

A study with a view of explaining the phenomena incidental to this case was undertaken in animals.

It often happens that various products having a therapeutic value when given subcutaneously are more prompt and extensive in their action when injected intravenously. This is true of many substances which produce a leucocytosis because of a high protein content as in the use of nuclein, blood sera, etc., so the question naturally arose in this connection, whether or not intravenous injections of leucocytic extract would produce an increase in the white blood count similar to that produced by a subcutaneous injection, inasmuch as it differs from the above noted products in not being dependent on its protein content for its action.

In order to clear this point up a series of rabbits were injected with the same lot of leucocytic

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extract, one-half being given a dose intravenously, the other half subcutaneously.

For the sake of illustration the following tables show the result of one of these experiments.

TABLE I.

Rabbit No. 5 was given two cubic centimeters leucocytic extract subcutaneously immediately after the first blood count was taken.

Time	W.B.C.	L.M.	S.M.	Poly	E.	B.
9:00 A. M.	7,200	13	47	36	4	0
11:00 A. M.	5,300	12	46	40	1	1
1:00 P. M.	8,500	4	36	59	1	0
3:00 P. M.	9,000	4	42	47	7	0
5:00 P. M.	16,200	10	18	68	4	0
7:30 P. M.	15,000	8	29	63	0	0
9:00 A. M.	10,300	12	34	47	7	0

TABLE II.

Rabbit No. 6 was given two cubic centimeters of the same lot of leucocytic extract as in the case of rabbit No. 5 intravenously.

Time	W.B.C.	L.M.	S.M.	Poly	E.	B.
9:00 A. M.	7,466	9	16	72	1	2
11:00 A. M.	13,600	16	8	75	1	0
1:00 P. M.	23,500	6	13	78	3	0
3:00 P. M.	18,200	10	18	62	10	0
5:00 P. M.	10,000	9	17	68	6	0
7:30 P. M.	6,000	9	24	63	4	0
9:00 A. M.	8,000	9	16	71	3	1

From the above experiments it will be observed that as a result of the injections of leucocytic extract of the same lot and under the same conditions into two rabbits the one intravenously and the other subcutaneously blood changes are obtained which are in a general way similar, but differ as to the rapidity and intensity with which the changes takes place.

In the case of the rabbit receiving the extract intravenously an increase in the total leucocyte count of one hundred per cent. occurred within two hours after injection, and the maximum of two hundred per cent. in the total leucocyte count was noted within four hours after injection. This count rapidly fell to a point slightly below the original count within ten hours after the dose was given, while with the rabbit given the same amount of the same lot of Leucocytic Extract subcutaneously no definite increase in the blood count was noted before the eighth hour, the maximum being reached about the tenth hour, with the count remaining considerably above the normal twenty-four hours after treatment.

In other words, when leucocytic extract is given intravenously a rapid and marked increase in the blood count is obtained with as rapid a drop to normal, while the administration of the same agent subcutaneously results in a slower and less marked reaction but one which is prolonged over a much greater period of time.

It occurred to us at this time that if magnesium sulphate was of benefit in connection with leucocytic extract that it might be profitable to make a combination of the two products during their manufacture thereby minimizing the technic of administration and at the same time exalting the potency of the leucocytic extract. It was reasoned that since magnesium sulphate was of such great assistance in leucocytotherapy that a saturation of leucocytic extract with magnesium sulphate might yield a product which, when diluted with three to four hundred cubic centimeters of water, would be ready for intravenous injection,

but upon animal experimentation such a combination was found to be inert.

Following this a study was made of the effect on animals of intravenous injection of these two agents simultaneously and this combination was also found to be unsatisfactory. On the other hand, a potent leucocytic extract injected subcutaneously together with an intravenous injection of magnesium sulphate always produced a marked reaction as did leucocytic extract and magnesium sulphate both given intravenously provided the two were injected at least one-half hour apart.

The following protocols demonstrate the above stated facts:

Rabbit No. 66 was given a mixture intravenously of 2 c.c. leucocytic extract in 40 c.c. of a 2% magnesium sulphate solution + 0.3 grams calcium chloride to the liter. Blood counts made at the 8th and 24th hours failed to show any effects upon the blood pictures.

Rabbit No. 67 was given simultaneously 2 c.c. Leucocytic extract subcutaneously and 40 c.c. of a 2% solution of magnesium sulphate + 0.3 grams calcium chloride to the liter intravenously. Blood counts made at the 8th and 24th hours showed a 100% increase in the total leucocyte count.

Rabbit No. 68 was given one-half hour apart 2 c.c. Leucocytic extract and 40 c.c. of a 2% magnesium sulphate solution + 0.3 grams calcium chloride to the liter intravenously. Blood counts made at the 8th and 24th hours showed a 100% increase in the total leucocyte count.

Rabbit No. 69 was given intravenously at the same time but not mixed 2 c.c. Leucocytic extract and 40 c.c. of a 2% magnesium sulphate solution + 0.3 grams calcium chloride to the liter. Blood counts made at the 8th and 24th hours failed to show any change in the blood pictures.

Rabbits Nos. 70 and 71 were given two cubic centimeters leucocytic extract subcutaneously and intravenously. Blood counts made at the 8th and 24th hours showed respectively 105% and 130% increase in the total leucocyte count.

In these experiments the reactions were at no time greater than the reaction obtained with leucocytic extract without magnesium sulphate but in a series of rabbits which had been intravenously injected with a laboratory strain of a staphylococcus aureus the leucocytosis was invariably highest in those rabbits receiving both leucocytic extract and magnesium sulphate, second in those receiving leucocytic extract alone and lowest in those receiving magnesium sulphate alone.

The following protocols bear out these facts:—

Rabbit No. 83 was given 0.5 c.c. of a twenty-four-hour old bouillon culture of a staphylococcus aureus intravenously. On the fourth day after infection this rabbit was given simultaneously 2 c.c. leucocytic extract subcutaneously and 40 c.c. of a 2% magnesium sulphate solution + 0.3 grams calcium chloride to the liter intravenously. Blood counts made at the end of twenty-four hours showed a 160% increase over the white blood count taken at the time the extract was injected, or 600% increase over the white blood count before infection.

Rabbit No. 84, infected with a staphylococcus aureus as in the case of Rabbit No. 83, was given 40 c.c. of a 2% solution of magnesium sulphate + 0.3 grams calcium chloride to the liter intravenously and one-half hour later 2 c.c. of leucocytic extract subcutaneously. Blood counts made at the end of twenty-four hours showed a 175% increase over the white blood count made at the time the

extract was injected or 500% increase over the white blood count before infection.

Rabbit No. 85 was given 2 c.c. leucocytic extract subcutaneously and Rabbit No. 86 2 c.c. of the same extract intravenously. These rabbits had also been infected with a staphylococcus aureus. Blood counts made at the end of twenty-four hours showed respectively a 100% and 75% increase in the white blood counts, or about the same increase over the white blood count before infection.

Rabbits Nos. 87 and 88, infected with a staphylococcus aureus, were each given 40 c.c. of a 2% magnesium sulphate solution + 0.3 grams calcium chloride to the liter. Blood counts made at the end of twenty-four hours failed to show any change in the blood pictures.

From these experiments it is obvious that the value of leucocytic extract is exalted many times by the magnesium sulphate which in itself has apparently no effect.

The reason for these phenomena seem quite evident. In the case of injection with leucocytic extract we are dealing with an agent which produces a leucocytosis and at the same time, by virtue of it, a marked increase in the proteolytic ferment content of the tissues and tissue juices. These ferments are normally present, not only for the purpose of splitting complex proteins which may be in the tissues as a result of pathological conditions but also in order to take care of the ordinary products of katabolism. Consequently when leucocytic extract is given to a normal animal the increase in ferment content increases the nitrogenous end products to a definite point beyond which it is impossible to go because of a lack of available protein on which the ferment may act. The leucocytosis appears in response to a demand created by these nitrogenous end products and is therefore limited. On the other hand when given to an individual suffering from an infectious disease or a toxemia there is a great mass of protein material, the result of tissue and bacterial destruction, which must be digested before elimination can take place. In this case, after a dose of leucocytic extract with its coincident increase in ferment, digestion goes on rapidly, large quantities of nitrogenous end products are liberated and a consequent increase in the leucocytes results.

It is obvious, therefore, that the more rapidly these are produced, the more rapidly elimination must take place else the normal balance will be lost and pathological accumulation will occur. Normal elimination is, however, decreased in patients suffering from acute infections and toxemias owing to a swelling of the parenchymatous tissues of the excretory organs, which swelling is the direct result of the acid end products upon the colloids of the body. The administration of leucocytic extract increases the tissue and blood ferments and hence causes a more rapid splitting of these foreign proteins. These substances must be removed from the body, however, before recovery is complete and it therefore follows that any procedure which will increase the intestinal and urinary output will make for a rapid recovery.

Now it is a well established fact that whereas

colloids, which in this case are the cells of the body, swell in the presence of all acids, this swelling is greatly inhibited if any salt be added to the acid solution, some salts being more efficacious in this regard than others. The most useful are the salts of magnesium, barium and calcium and of these the sulphates rather than the others, hence in magnesium sulphate we have a salt ideal in its power to inhibit the above mentioned action of acids on colloids. In this particular instance we have the kidneys, intestines, etc., on whose excretory powers there is a very heavy demand so altered by these end products as to markedly reduce their functioning power. The intravenous injection of magnesium sulphate inhibits the swelling of the kidneys, increases the urinary output and thus disposes of the waste, which permits the ferment, produced by leucocytic extract, to complete the cycle of its digestion.

In addition to the case of streptococcemia already mentioned the following are a few case reports selected at random showing the clinical application of the above outlined theories.

*Japanese woman.*—Five months pregnant, developed an acute pyelitis with marked constitutional symptoms. During the course of the pyelitis a colon bacillus septicemia developed. The administration of leucocytic extract subcutaneously and magnesium sulphate intravenously was begun immediately after two different blood cultures had shown the presence of a colon bacillus. Two cubic centimeters of leucocytic extract were given subcutaneously daily, while four hundred cubic centimeters of a two per cent. magnesium sulphate solution was administered intravenously every third day, three injections being given in all. A blood culture taken after the final injection of magnesium sulphate was sterile.

Mrs. B., puerperal sepsis. Chill and temperature of 104° on third day after confinement with a streptococcus present in large numbers within the uterus. Patient prostrate, appearing very ill. Leucocytic extract was given subcutaneously immediately followed in a few hours by 350 c.c. of a 2% magnesium sulphate solution intravenously. The temperature fell to 99° in the next twenty-four hours, leucocytic extract was continued daily and a second and last dose of magnesium sulphate was given two days later. In less than eighteen hours the temperature reached normal, where it remained, the patient making an uneventful recovery.

The clinical history of many other cases similarly treated could be recited but it is believed that the above will suffice to demonstrate that in the treatment of bacteremias the combined use of leucocytic extract and magnesium sulphate solution is worthy of serious consideration.

#### SUMMARY.

While beneficial results may be obtained from the use of leucocytic extract and magnesium sulphate solution alone, much more gratifying results are obtained by their joint use, provided, that if they are administered simultaneously the extract be given subcutaneously and the salt solution intravenously. If, however, both are given intra-

venously one-half hour at least must be allowed to elapse between the administration of each.

Leucocytic extract given intravenously gives its maximum white blood count in four hours after injection, while the subcutaneous injection shows the maximum increase from the eighth to the tenth hour. It was also demonstrated that the leucocytic increase following intravenous injection is more transient than when administered subcutaneously.

It is apparent that the joint action of the leucocytic extract and magnesium sulphate solution is intensified when administered in a bacteremic condition more so than in a normal individual.

In the treatment of all bacteremias the combined use of leucocytic extract and magnesium sulphate solution has proven to be more efficacious than any other treatment heretofore devised.

### INTESTINAL CRISES SIMULATING CHRONIC APPENDIX DISEASE DIAGNOSED BY ROENTGEN RAY FINDINGS.\*

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The marked obscurity of diagnosis in this case, which was finally cleared up by Roentgen findings, demonstrates quite clearly the value of the Roentgen examination as a "dernier ressort" method of diagnosis in all dubious abdominal complaints.

Mr. H. came under observation last February and had then been ill for a period of thirteen months. Age 45, unmarried. Occupation, a farmer, but had been in the liquor business for several years. States that during this time he had been a heavy consumer of alcohol in all forms.

Thirteen months before coming under our observation, he had consulted several local physicians, who had told him he was suffering from bright's disease and treated him for such, but showing no improvement he then consulted another physician in the same locality, who treated him symptomatically. Again not improving under this course of procedure, he consulted one of us. The following history was obtained:

The patient had always been a perfectly healthy man up to January, 1915. Somewhere about the first of January, 1915, he began to complain of a burning, scalding sensation in the eyes, which was attended with considerable lacrymation. Much stress was laid on this symptom by the patient and he stoutly persisted that every abdominal attack which he has had was always preceded by this phenomenon. Simultaneously with these morbid manifestations, he complained of jerking in the facial muscles, accompanied by severe pain, which he described as rheumatic in character. He was also troubled with severe pharyngitis. About one week later he developed severe gas pains, coming on about noon, some six hours after eating his first meal of the day. They were so severe that he was unable to lie down, but forced to sit up

for long periods of time as lying down caused him severe palpitation of the heart.

Three days after the onset of the gas disturbance he had a severe attack of terrible gripping pains throughout the bowel, radiating to the lumbar region of the spine. This attack lasted over a period of two weeks. For several days following this attack he was free from pain. He states that he was always constipated before these attacks came on. Enemas and strong cathartics were of no value. His stools were usually quite dark and never clay colored. These attacks, always similar in character, occurred quite regularly about once a week up to about one month before consulting us.

A short time prior to his arrival here, he remembers that three hours after taking some medicine prescribed by his local doctor, he became distinctly nauseated, developing severe pain in the right side, accompanied by a frontal headache and later on vomited. For a period of twenty-four hours these attacks were repeated, the colics on the right side lasting from fifteen to twenty minutes. Prior to this time he had noticed that he had been troubled with cramps in the region of the appendix, but had paid no attention to it.

In describing his attacks of intestinal pain associated with gas, he stated that he was obliged to urinate every hour during the night and day. Ordinarily he would only urinate four or five times during the day and never during the night. For the past year he has complained of being constantly chilled. He has lost ten pounds since the attacks first came on.

Past history: States he had gonorrhea nine years ago, but denies ever having syphilis. He had malaria eight years ago, otherwise he has been a robust, healthy man until afflicted with his present trouble.

Family history: Negative. Mother is well. Father died of old age. Several brothers and sisters living, who are all well.

Habits: Has been a heavy drinker prior to one year ago, also a consumer of about fifteen cigarettes a day for about twenty-five years. Physical examination revealed a slight amount of tenderness over the region of the appendix, otherwise negative.

Fundi were negative, both discs being distinctly outlined with no signs of inflammation. Pupils reacted to both light and accommodation. The left pupil was somewhat sluggish and resembled the springy pupil.

Nose and throat, chest and heart all negative.

Nervous system: No Romberg or Babinsky sign. Knee jerks were slightly increased. Achilles tendon reflex normal.

Genito-urinary examination revealed large glands in groins and an old chronic gonorrhea, complicated with several strictures. Otherwise his physical examination was negative.

Laboratory examination:

Blood pressure—maximum 140, minimum 90.

Hemoglobin 80.

Red cells 4,500,000.

White cells 5,900.

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